EXHIBIT D

Recovery G2 Inferior Vena Cava Filter: Technical Success and Safety of Retrieval

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PURPOSE: To assess the safety and technical success of the retrieval of the Recovery G2 filter when implanted for temporary protection against pulmonary embolism.

MATERIALS AND METHODS: The Recovery G2 inferior vena cava (IVC) filter was placed in 120 consecutive patients between September 2005 and September 2006 in a single center. Patients had deep venous thrombosis (DVT) (n = 63), pulmonary embolism and DVT (n = 55), and high risk for pulmonary embolism without recent thromboembolic disease (n = 2). Indications for filter placement included contraindication to anticoagulation (n = 106), failure of anticoagulation (n = 11), and prophylaxis in addition to anticoagulation (n = 3). In patients eligible for filter removal, the authors measured the mean implantation time, filter retrieval success rate, and retrieval procedure time. In addition, they assessed filter tilting, migration, caval penetration, thrombus within the filter, fracture, and caval injury or stenosis.

RESULTS: In the 51 patients who met the criteria for filter removal, filter tilting (>15°) was seen in six patients (12%), small thrombi were seen in filters of 15 patients (29%), presumed caval penetration was seen in nine patients (18%), and caudal filter migration was seen in two patients (3.9%). There were no fractures or cephalic migrations. Removal attempts were successful in all 51 patients (100%). The mean implantation time was 53.4 days (range, 7–242 days), and the retrieval procedure time averaged 16.8 minutes (range, 5–60 minutes).

CONCLUSIONS: Retrieval of the Recovery G2 filter is safe and can be performed successfully in patients who no longer need IVC filtration.

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Abbreviations: DVT = deep venous thrombosis, IVC = inferior vena cava

PERMANENT inferior vena cava (IVC) filters have been associated with various complications, including venous thrombosis, filter obstruction, filter fracture with embolization, migration, and caval penetration (1–4). Although the rate of clinically meaningful complications associated with permanent filters is low, some of these complications can presumably be avoided by using a retrievable filter in patients who have limited temporal requirements for IVC filtration (5–7). Such a device is the Recovery G2 filter (Bard Peripheral Vascular, Tempe, Arizona), which is an evolution of the Recovery filter (Bard Peripheral Vascular) (8). Its design was modified in an attempt to decrease the occurrence of fatigue-related fractures, minimize IVC penetration, decrease the occurrence of tilting, and increase the resistance to migration while maintaining its extended retrievability period. The goal of the present study was to evaluate the retrievability of the Recovery G2 filter in patients who no longer require IVC filtration.

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MATERIALS AND METHODS

Study Design

One hundred twenty consecutive patients underwent placement of a Recovery G2 filter at our hospital between September 2005 and September 2006. The patients included 70 women and 50 men with an average age of 63.5 years (range, 20–92 years), and they had an indication for placement of an IVC filter according to the Society of Interventional Radiology guidelines (9,10). Filters were placed in these patients without the need for a specific intent to retrieve them. The status of their thromboembolic disease was as follows: 63 of the 120 patients (52.5%) had deep venous thrombosis (DVT), 55 (45.8%) had pulmonary embolism with or without DVT, and two

(1.7%) had a history of DVT with no evidence of recent thromboembolic disease. The patients were all considered at risk for pulmonary embolism by their referring physician, and IVC filtration was indicated for contraindication to anticoagulation in 106 patients (88.3%), failure of anticoagulation in 11 (9.2%), and prophylaxis in addition to anticoagulation in three (2.5%). Of these 120 patients in whom a Recovery G2 filter was placed, 51 patients met the following criteria for filter removal: (*a*) the filter was no longer required, (*b*) anticoagulation could be resumed, and (*c*) the filter was free of large trapped thrombus. Herein, we focus on the 51 patients in whom filter retrieval was attempted. Institutional review board approval was obtained for this prospective study.

Device

The Recovery G2 filter is an evolution of the first-generation Recovery nitinol filter (Fig 1). The design modification objectives and features of the device are detailed in **Table 1**.

The Recovery G2 filter is composed of 12 0.013-inch nitinol wires that join at the apex of the device. Six of these wires measure 19.8 mm in length and form the arms. The remaining six wires have anchoring hooks at their tips and form the legs. The resting leg span is 40 mm, and the filter measures 40 mm in height. The maximum indicated vessel diameter remains at 28 mm. Table 2 summarizes the key distinguishing features of the original Recovery versus Recovery G2 filters.

Insertion Technique

An inferior vena cavogram was obtained with a femoral or jugular approach. The filter was advanced percutaneously by means of the same route through a 7-F femoral or 10-F jugular introducer catheter. A flexible nitinol pusher was used to advance the filter to the distal end of the catheter so that the filter was positioned between the radiopaque markers on the introducer catheter. The introducer catheter and delivery assembly were then pulled back onto the nitinol pusher handle to unsheath and release the filter into the IVC below the renal veins.

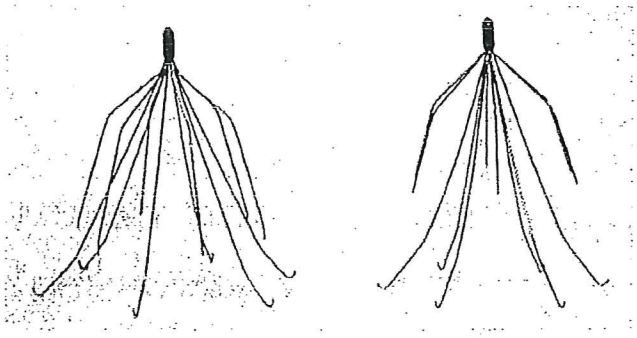

Figure 1. Recovery G2 filter (left) and original Recovery filter (right). The Recovery G2 filter has a wider leg span, longer arms with inward curve and progressive angle of wires exiting the tip compared to the original Recovery filter.

Retrieval Procedure

An inferior vena cavogram was initially obtained with a jugular approach to identify filter position and assess the presence of trapped thrombus. If patients met the criteria for filter removal according to the study design, a Recovery cone removal system (Bard Peripheral Vascular) was advanced through a 10-F jugular introducer catheter over the apex of the filter (**Fig 2**). If substantial filter tilting was present, a 260-cm-long Amplatz wire (Cook, Bloomington, Indiana) was initially positioned into the IVC below the filter, toward the side where the shortest distance is seen between the filter tip and the caval wall (Fig 3).This technique facilitates the docking procedure by advancing the retrieval cone over the Amplatz wire. The introducer sheath was then used to collapse the removal cone over the filter tip, and the filter was removed from the patients by pulling the filter and collapsed cone into the sheath as a unit. After filter removal, a repeat inferior vena cavogram was obtained to assess the IVC for injury.

Study Endpoints

The primary endpoint of our study was the retrieval of the filter without major complications.

The following secondary endpoints were also evaluated: mean implantation time, filter retrieval success rate, retrieval procedure time (the time between preretrieval cavography to postretrieval cavography), filter tilting (substantial if more than 15° from the long axis of the IVC), migration (change in cephalocaudal position greater than 2 cm), presumed caval penetration (struts extending more than 3 mm outside the contrast medium–filled IVC lumen), thrombus within the filter (small: less than half of the filter basket; large: more than half of the filter basket), fracture (any loss of structural integrity of the filter), caval stenosis or occlusion (at least 50%), and caval perforation (loss of integrity of the IVC wall with extravasation of contrast medium).

RESULTS

Filter Insertion Procedure

IVC filters were inserted from the right common femoral vein in 101 patients, from the left common femoral vein in 18 patients, and from the right internal jugular vein in one patient. All patients had their filter successfully placed in the infrarenal IVC without procedural complications.

Retrieval Procedure

Of the 120 patients who had received a Recovery G2 filter during the study period, 59 underwent diagnostic vena cavography for the purpose of assessing filter retrievability. Large trapped thrombi within the filter were found in eight of these 59 patients, and, consequently, 51 of the initial 120 patients (42.5%) met the criteria for filter retrieval.

Filter removal was not attempted in 69 patients as a result of ongoing contraindication to anticoagulation (n = 40), prolonged need for prophylaxis

Table 1
Design Modifications of Recovery G2 Filter Relative to Original Recovery Filter

Objective	Feature	Mechanism
Increased Migration Resistance	Wider leg span	Accommodate greater vessel distention.
	Stronger hooks	Larger diameter wire at level of hooks leads to stronger fixation.
Reduced Tilt	Longer arms	Provides a more axially-oriented support.
	Curved arm ends	Inward angle reduces the likelihood of arm penetration.
Increased Fracture Resistance	Progressive wire angle	Reduces the load to the arms as they exit the tip.
	Longer arms	Evenly distributes the load and reduces stress on wires.
	Curved arm ends	Reduces the likelihood of penetration and, therefore, less fatigue on wires.

Table 2
Characteristics of Recovery G2 versus Original Recovery Filter

Characteristic	Recovery Filter	Recovery G2 Filter
Height (mm)	41	40
Leg span (mm)	32	40
Hook thickness (mm)	0.216	0.267
Arm length (mm)	11.3	19.8
Arm ends	Straight	Curved

against pulmonary embolism ($n = 12$), large trapped thrombi within the filter ($n = 8$), poor patient prognosis ($n = 4$), and death ($n = 5$). No death or adverse event was attributable to the IVC filter in these patients.

All 51 patients who met the criteria for filter removal had their filter successfully retrieved with no associated adverse events, for a retrieval success rate of 100%. The mean interval (± standard deviation) between filter implantation and retrieval was 53.4 days ± 44.2 (range, 7–242 days). The mean retrieval procedure time was 16.8 minutes ± 6.3 (range, 5–60 minutes).

Of the 51 patients who had their filter successfully retrieved, small thrombi were identified at cavography within the filter of 15 patients (29%). Filter removal was performed with a standard technique in these patients. Strut penetration was observed in nine of the 51 patients (18%) as follows: a single strut (one arm or one leg) had penetrated the IVC wall in four patients, and multiple struts had penetrated the IVC wall in five patients. A total of eight filter arms and nine filter legs had penetrated the IVC wall in these nine patients. Filter tilting (more than 15° from the axis of the IVC) was present in six of the 51 patients (12%), four of whom also had concomitant strut penetration. Filter removal was performed successfully in all patients in whom tilting and/or strut penetration was observed, and they were all asymptomatic.

Caudal migration of the Recovery G2 filter was observed in two patients. In the first case, the cavogram obtained immediately before retrieval and 149 days after filter placement revealed a 2.5-cm caudal migration without associated tilting or strut penetration. In the second patient, a 2-cm caudal migration was observed 28 days after filter insertion. Penetration of one arm and one leg was also present without substantial tilting. In both cases, the patients were free of symptoms and the filters were removed uneventfully. No cephalad filter migration was observed in our series. There were no occurrences of filter fracture, and no IVC injury was identified during or after filter removal.

DISCUSSION

Considering the risks associated with long-term IVC filtration (3,11,12), optional or retrievable filters have become increasingly popular. Because changing clinical circumstances can affect the required duration of filtration, optional filters that can be removed after long dwell times facilitate the treatment of patients with venous thromboembolic disease. The first-generation Recovery filter incorporated elastic leg hooks into its design, thus providing extended optional IVC filtration (8,13). However, this first-generation filter was redesigned because of concerns about strut fracture and migration (14,15). The new design of the Recovery G2 filter includes thicker leg hooks, a wider leg span, and longer arms with a more progressive angle of the wires forming the arms at the filter apex with inward curve at their end. These modifications were aimed at reducing the occurrence of filter migration, fracture, and tilting without compromising the ability to retrieve the filter. The increased resistance to cephalic migration was achieved by increasing the diameter of the hook wires to decrease their deformability, thus leading to more rigid fixation. The main objective of our study was to evaluate whether the new characteristics of the Recovery G2 filter would compromise its retrievability. In the present series, filter removal was successful in all 51 patients in whom filter removal was attempted, with a mean dwell time of 53.4 days (range, 7–242 days). These results confirm the extended retrievability of the G2 filter despite the design changes as compared with the first generation Recovery filter. Eight of the 120 patients had large thrombi within their filter at follow-up cavography, which was defined as thrombus that occupied more than half of the filter basket. This was considered a contraindication to filter removal in our study, and because removal was

a. b. c. d.

Figure 2. (a) Vena cavogram obtained with a right jugular approach in 74-year-old man with lower extremity DVT. Anticoagulation was resumed after abdominal surgery. The Recovery G2 filter is in a good position below the renal veins. Notice the absence of thrombus in the filter. (b) Retrieval cone in an open position above the apex of the filter. (c) Recovery G2 filter is being pulled into the retrieval sheath. (d) Follow-up vena cavogram obtained through the retrieval sheath after filter removal reveals no caval abnormality.

not attempted in these patients, these were not considered a filter removal failure.

The filter retrieval procedures were easy and straightforward in the overwhelming majority of cases, with a mean procedural time of 16.8 minutes. Substantial tilting, defined as more than 15° relative to the long axis of the IVC at cavography, was observed in six of 51 patients in whom filter removal was attempted (12% tilt rate). In these six patients, filter tilting was observed in the presence of at least one filter strut that projected outside the IVC wall, either due to caval penetration (four patients) or a strut sitting in a renal or lumbar vein (two patients). However, penetration of the caval wall was not always associated with filter tilting in our series as this was observed in five patients without tilted filters.

When a substantial tilt was present, we used a retrieval technique originally described by Asch (8), which involves the use of an angled catheter to manipulate a wire toward the side of the filter tilt between the filter apex and the IVC wall. The retrieval cone is then inserted over the wire, which facilitates the docking procedure. Another technique described by Hagspiel et al (16) for removing tilted Recovery filters involves the use of a tip-deflecting wire inserted through the central lumen of the retrieval cone. This method enables centering of the filter within the IVC by activating the guide wire tip deflection without the need to remove the retrieval cone or perform a catheter exchange.

The longest retrieval procedure in our series (60 minutes) occurred in a 25-year-old patient (**Fig 3**) with DVT and temporary contraindication to anticoagulation due to surgery. After anticoagulation was resumed, severe tilting of the filter with penetration of two filter legs was documented at CT. Considering the young age of the patient, it was decided to attempt filter removal. The retrieval procedure was performed with a right jugular approach, and the preretrieval cavogram helped confirm penetration of two legs with a 32° tilt of the filter with apparent contact between the filter apex and the caval wall. The dwell time of the filter in this patient was 128 days. As described earlier, a guide wire inserted through a 5-F angled catheter was manipulated between the filter apex and the IVC wall immediately below the embedded tip. The Recovery cone was then placed over the wire, and the apex of the filter was eventually mobilized away from the caval wall, thus allowing the filter to be removed without complication. In this particular case, the procedure required lengthy manipulations—especially for placing the guide wire toward the side of the filter tilt—because the tip was embedded in the caval wall. This is the only case of filter tip embedment observed in our series, and all the other retrievals were uneventful—including those performed in cases where tilting or strut penetration was present. Although all retrieval attempts were successful in our study, extreme filter tilting could lead to retrieval failure. On the basis of past experience with the Recovery filter, attempts to straighten tilted filters can fail despite the use of catheters and wires, snares, and tip-deflecting wires (17,18). In these cases, it is likely that the tip of the filter is embedded in the caval wall, which can compromise filter removal. When caval wall incorporation of the filter occurs, Stavropoulos et al (19) have described the use of bronchoscopy grasping forceps to dissect the tissue around the embedded filter apex. This fairly aggressive technique enabled the Recovery filter to be

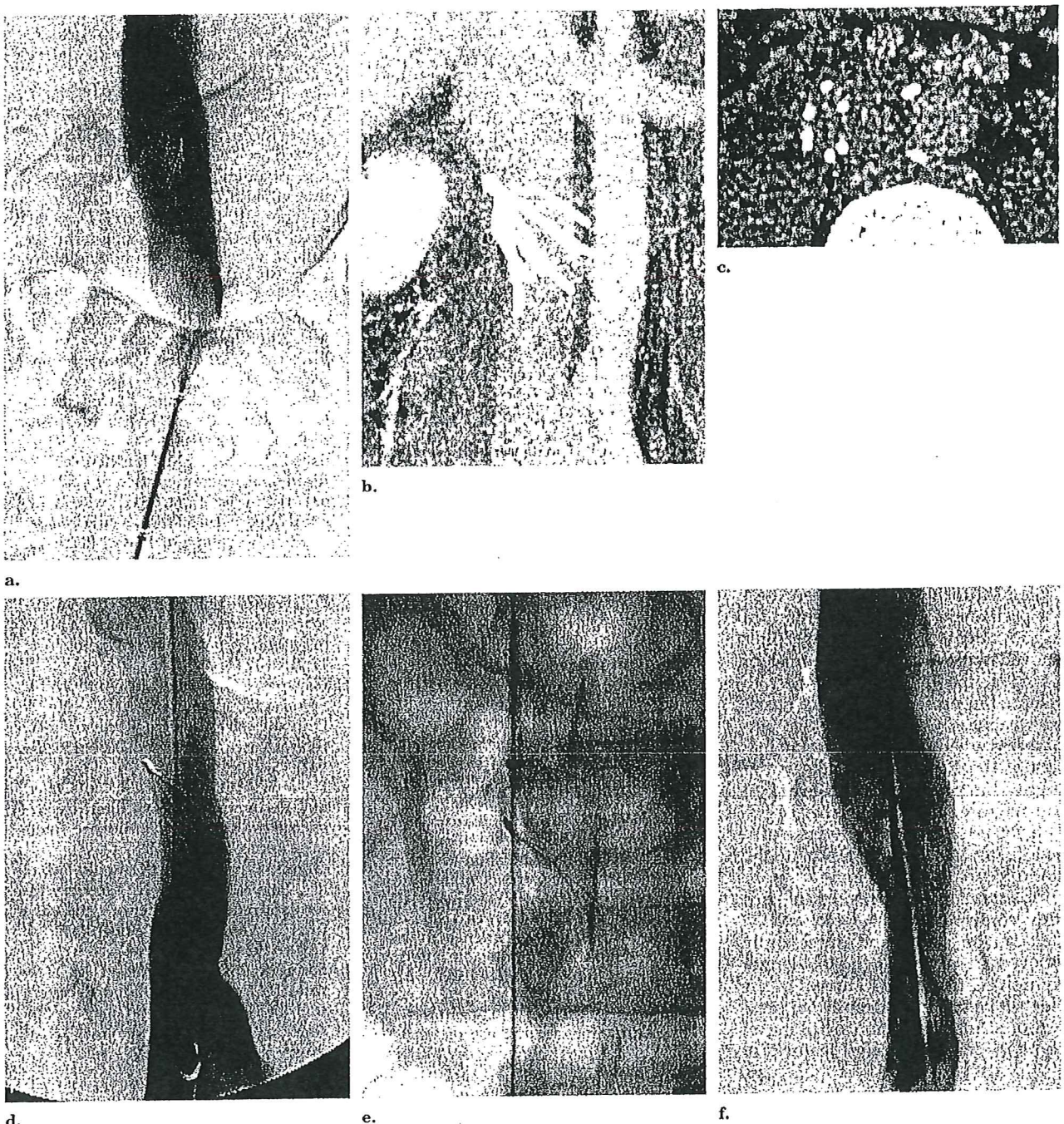

Figure 3. (a) Inferior vena cavogram obtained after placement of the Recovery G2 filter in an adequate position in 25-year-old man with lower extremity DVT and temporary contraindication to anticoagulation. (b) Coronal reconstruction of a computed tomographic (CT) scan obtained 2 months after filter placement. There is absence of entrapped thrombus; however, severe tilting of the filter is observed and caval penetration of filter struts is suspected. (c) Axial CT scan helps confirm the penetration of two filter legs that lie in close contact with the abdominal aorta. (d) Angiogram of the IVC before filter removal helps confirm severe tilting of filter. (e) On digital radiograph, an Amplatz wire has been placed toward the side where the shortest distance is present between the filter apex and the caval wall to guide the retrieval cone to the filter apex. (f) Follow-up vena cavogram obtained after filter removal reveals the absence of caval injury.

safely removed in four patients in their series.

We observed two cases of caudal migration of the Recovery G2 filter in our study. Although the exact mechanism for these migrations is unclear, we believe that the new design of this device could be a factor in these events. Indeed, the arms of the Recovery G2 filter have been extended and curved inward to minimize caval penetration and, as a result, are less likely to catch on the IVC wall. This may facilitate caudal movement of the filter, which may be submitted to a ratcheting effect from the dynamic motion of the IVC. The occurrence of caudal migration was asymptomatic and did not compromise the filter retrieval procedure in these two cases.

There are limitations to our study. This report focused on the retrievability of the Recovery G2 filter, and no systematic imaging follow-up was performed in patients in whom the filter was left in place. As such, we cannot evaluate the safety and performance of this new device when used as a permanent filter. In addition, in the 51 patients who had their filter removed with a mean dwell time of 53.4 days, the delay is too short to evaluate the presence of device structure weakness. Consequently, we cannot assess whether the new design features of the Recovery G2 filter were effective in preventing the event of strut fracture, and the number of patients included in our study is insufficient to assess the resistance of the filter to cephalic migration.

In summary, the results of this study confirm that the Recovery G2 filter can be safely and successfully retrieved in patients who no longer require IVC filtration. Removal of the filter can be achieved despite the presence of strut penetration or tilting of the filter. The new design features of this filter, which were aimed at reducing the occurrence of cephalic migration and strut fracture, do not seem to compromise the ability to remove the filter after long dwell times. However, the long-term resistance of the Recovery G2 filter to cephalic migration and structural fracture will require further evaluation.

References

1. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. N Engl J Med 1998; 338:409–415.
2. Ferris EJ, McCowan TC, Carver DK, McFarland DR. Percutaneous inferior vena caval filters: follow-up of seven designs in 320 patients. Radiology 1993; 188:851–856.
3. Kinney TB. Update on inferior vena cava filters. J Vasc Interv Radiol 2003; 14:425–440.
4. Kaufman JA, Thomas JW, Geller SC, Rivitz SM, Waltman AC. Guide-wire entrapment by inferior vena caval filters: in vitro evaluation. Radiology 1996; 198:71–76.
5. Millward SF, Oliva VL, Bell SD, et al. Gunther Tulip retrievable vena cava filter: results from the registry of the Canadian interventional radiology association. J Vasc Interv Radiol 2001; 12: 1053–1058.
6. Yamagami T, Kato T, Lida S, Tanaka O, Nishimura T. Retrievable vena cava filter placement during treatment for deep venous thrombosis. Br J Radiol 2003; 76:712–718.
7. Oliva VL, Szatmari F, Giroux MF, Flemming BK, Cohen SA, Soulez G. The Jonas study: evaluation of the retrievability of the Cordis OptEase inferior vena cava filter. J Vasc Interv Radiol 2005; 16:1439–1445.
8. Asch MR. Initial experience in humans with a new retrievable inferior vena cava filter. Radiology 2002; 225: 835–844.
9. Kaufman JA, Kinney TB, Streiff MB, et al. Guidelines for the use of retrievable and convertible vena cava filters: report from the Society of Interventional Radiology multidisciplinary consensus conference. J Vasc Interv Radiol 2006; 17:449–459.
10. Grassi CJ, Swan TL, Cardella JF, et al. Quality improvement guidelines for percutaneous permanent inferior vena cava filter placement for the prevention of pulmonary embolism. J Vasc Interv Radiol 2003; 14:S271–S275.
11. Crochet DP, Stora O, Ferry D, et al. Vena-Tech-LGM filter: long-term results of a prospective study. Radiology 1993; 188:857–860.
12. Joels CS, Sing RF, Heniford BT. Complications of inferior vena cava filters. Am Surg 2003; 69:654–659.
13. Binkert CA, Sasadeusz K, Stavropoulos SW. Retrievability of the recovery vena cava filter after dwell times longer than 180 days. J Vasc Interv Radiol 2006; 17:299–302.
14. Saeed I, Garcia M, McNicholas K. Right ventricular migration of a Recovery IVC filter's fractured wire with subsequent pericardial tamponade. Cardiovasc Intervent Radiol 2006; 29: 685–686.
15. Ganguli S, Tham JC, Komlos F, Rabkin D. Fracture and migration of a suprarenal inferior vena cava filter in a pregnant patient. J Vasc Interv Radiol 2006; 17:1707–1711.
16. Hagspiel KD, Leung DA, Aladdin M, Spinosa DJ, Matsumoto AH, Angle JF. Difficult retrieval of a Recovery IVC filter. J Vasc Interv Radiol 2004; 15:645–647.
17. Kalva SP, Athanasoulis CA, Fan CM, et al. Recovery vena cava filter: experience in 96 patients. Cardiovasc Intervent Radiol 2006; 29:559–564.
18. Grande WJ, Trerotola SO, Reilly PM, et al. Experience with the Recovery filter as a retrievable inferior vena cava filter. J Vasc Interv Radiol 2005; 16: 1189–1193.
19. Stavropoulos SW, Solomon JA, Trerotola SO. Wall-embedded Recovery inferior vena cava filters: imaging features and technique for removal. J Vasc Interv Radiol 2006; 17:379–382.